USEFULNESS OF $^{99m}$Tc PYROPHOSPHATE BONE SCINTIGRAPHY IN THE SURVEY OF DIALYSIS OSTEODYSTROPHY

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Summary

Fogelman’s score (FS) was used to determine the usefulness of $^{99m}$Tc pyrophosphate (Tc-PP) bone scintigraphy in the evaluation of dialysis osteodystrophy. FS correlated well with bone $^{47}$Ca accretion rate. It remained stable after six months in patients treated with 1α(OH)D$_3$ and increased significantly in a randomised group of untreated patients. It decreased after two years of 1α(OH)D$_3$ therapy while serum calcium increased and iPTH and alkaline phosphatases decreased. Patients with low FS, treated by 1α(OH)D$_3$, rapidly developed hypercalcaemia. In cases of spontaneous hypercalcaemia, parathyroidectomy did not normalise serum calcium in patients with low FS despite a significant decrease in serum iPTH. Lower FS were associated with a higher increase in serum aluminium after desferrioxamine (DFO) administration and in two cases of proven aluminium osteomalacia, DFO therapy was followed by a dramatic increase in FS.

Introduction

After five years of dialysis, about 15 per cent of patients present with a severe disabling bone disease [1]. For early diagnosis, X-rays are disappointing since the radiological signs are often late. Histological examination is certainly the most accurate method but bone biopsies may obviously not be done repeatedly in asymptomatic patients. As bone scintigraphy was shown to be a sensitive method for revealing renal osteodystrophy [2–5] we decided to evaluate the systematic use of this technique in a survey of dialysis patients.

Methods

Bone scintigraphy was performed four hours after an IV injection of $^{99m}$Tc pyrophosphate (Tc-PP). A dialysis session was systematically begun 30 minutes
after the injection of the tracer and ended before scan imaging [5]. Bone uptake of Tc-PP was estimated semi-quantitatively according to Fogelman [6]. Six areas of interest were examined and Tc-PP uptake of each area was scored from 0 to 2, giving a global Fogelman’s score (FS) from 0 to 12. Very poor uptake by bone scored 0. Bone scintigraphy was routinely done every six months in all dialysed patients. The following data were retrospectively recorded:

1. In 11 patients, FS was correlated with the bone calcium accretion rate calculated from the radiocalcium retention and the plasma radioactivity curve recorded during seven days following IV injection of $^{47}$CaCl$_2$ [7].

2. The significance of FS as an index of bone disease activity was assessed
   a) by comparing FS of 12 patients treated by 1α(OH)D$_3$ (1μg/d) to FS of nine patients treated by placebo, in correlation with biological parameters of bone disease
   b) by correlating the evolution of FS in 14 patients after two years of 1α(OH)D$_3$ therapy to that of the biological parameters of bone disease.

3. The predictive value of Tc-PP bone scintigraphy was analysed
   a) by comparing the FS of 10 patients who developed an increase in serum calcium above 11mg/dl in the course of the first month of 1α(OH)D$_3$ therapy (1μg/d) to the FS of 10 patients who tolerated the treatment
   b) by comparing the FS of 13 patients whose serum calcium fell after parathyroidectomy performed according to Wells [8] to the FS of two hypercalcaemic patients who did not respond to parathyroidectomy.

4. The value of Tc-PP bone scintigraphy in aluminium bone disease was examined
   a) by correlating FS and the increase in serum aluminium after the IV administration of 1g desferrioxamine (DFO)
   b) by observing the changes in Tc-PP bone uptake during DFO therapy in two cases of histologically proven aluminium bone disease.

Results

1. In 11 dialysed patients, there was a good correlation between FS and bone $^{47}$calcium accretion rate ($r = 0.80$, $p < 0.01$).

2. a) Table 1 shows the significant difference in the evolution of FS, iPTH, serum calcium and alkaline phosphatases in two groups of dialysed patients (a group treated by 1α(OH)D$_3$ and a control group treated by placebo). After six months, FS remained stable in 12 patients treated by 1α(OH)D$_3$ while it significantly increased in nine control patients treated by placebo.
   b) In 14 patients treated with 1α(OH)D$_3$ for two years, FS decreased from 8.4 ± 0.6 to 5.3 ± 0.4 ($p < 0.001$) while serum calcium rose from 8.5 ± 0.2 to 10.3 ± 0.1mg/dl ($p < 0.001$) with a concomitant decrease in iPTH (from 84 ± 6 to 59 ± 4μEq/ml, $p < 0.001$) and in alkaline phosphatases (from 84 ± 12 to 41 ± 3UI/ml, $p < 0.01$).
TABLE 1. Evolution of the signs of metabolic bone disease activity in dialysed patients treated by 1α(OH)D₃ as compared to a placebo group (after six months)

<table>
<thead>
<tr>
<th></th>
<th>1α(OH)D₃ (n = 12)</th>
<th>placebo (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variations expressed in percent of basal values:</td>
<td></td>
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<tr>
<td>iPTH</td>
<td>−34 ± 9</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Alkaline phosphatases</td>
<td>−45 ± 21</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Serum calcium</td>
<td>+24 ± 5</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Fogelman’s score</td>
<td>−8 ± 8</td>
<td>p≤0.05</td>
</tr>
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</table>

3. a) Thirty-eight dialysed patients received oral calcium supplements (calcium carbonate 1.8g/d) and 1α(OH)D₃ (1μg/d). The calcium dialysate content was 7.5mg/dl. Ten of these patients developed hypercalcaemia (serum calcium above 11.0mg/dl) in the course of the first month of therapy while the 23 other patients tolerated the treatment well. The former had lower FS (3.6 ± 0.8) as compared to the latter (8.0 ± 0.4) (p < 0.001).

b) In 13 patients with high FS (9.2 ± 0.5), parathyroidectomy was followed by a prompt decrease in serum calcium from 10.7 ± 0.3 to 8.0 ± 0.4mg/dl. On the opposite, in two patients with low FS (1.0 ± 0.0), parathyroidectomy did not correct hypercalcaemia (11.0 ± 0.5mg/dl before and after surgery) despite a significant reduction of iPTH. Further investigations demonstrated that these two patients had bone aluminium intoxication.

4. a) After administration of DFO, the increase in serum aluminium was significantly (p < 0.001) higher (Δ = 100.9 ± 18.5μg/L) in seven patients with low FS (3.3 ± 0.3) than in 17 patients (Δ = 42.1 ± 9.2μg/L) with greater FS (6.8 ± 0.3, n = 17).

b) In two patients with histologically proven aluminium bone disease the Tc-PP bone uptake was very poor. After some weeks of DFO therapy, FS increased to 8–9 while the clinical condition improved dramatically.

Discussion

Tc-PP bone scintigraphy was suggested to be a sensitive method for detecting early stages of metabolic bone disease in renal failure [2–5]. Tc-PP bone uptake seems indeed related to the calcium bone turnover as suggested by our data. FS correlated with radio calcium accretion rate as well as with biological parameters of metabolic bone disease activity. Moreover, treatment with an active vit D
metabolite which is supposed to decrease the activity of the disease, reduced Tc-PP bone uptake.

If FS correlates with calcium accretion rate, the patients with low FS are expected to develop rapidly hypercalcaemia during an exogenous calcium load. Indeed, our previous suggestion [9] that Tc-PP bone scintigraphy could be useful for detecting uraemic patients at risk for vitamin D intoxication is confirmed by the present data in a larger group of patients. On the other hand, the effect of parathyroidectomy in patients with spontaneous hypercalcaemia can be predicted by FS. A low FS suggests that parathyroidectomy will fail to decrease serum calcium. Finally, a poor Tc-PP bone uptake may also suggest a blockade in bone mineralisation due, for instance, to aluminium intoxication [10].

In conclusion, Tc-PP bone scintigraphy is an easy non-invasive technique that may be useful 1) to diagnose early bone diseases in uraemic patients, 2) to evaluate the degree of disease activity and the effects of a treatment, 3) to detect the patients at risk for vitamin D intoxication, 4) to discuss the indications of parathyroidectomy especially in cases of spontaneous hypercalcaemia and 5) to detect the patients with a blockade in bone mineralisation such as aluminium intoxication.

References

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